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Moxifloxacin

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Contents

Abstract

▲ Moxifloxacin is a new fluoroquinolone antibacterial agent with a broad spectrum of activity, encompassing Gram-negative and Gram-positive bacteria. It has improved activity against Gram-positive species (including staphylococci, streptococci, enterococci) and anaerobes compared with ciprofloxacin. This is offset by slightly lower activity against pseudomonal species and Enterobacteriaceae.

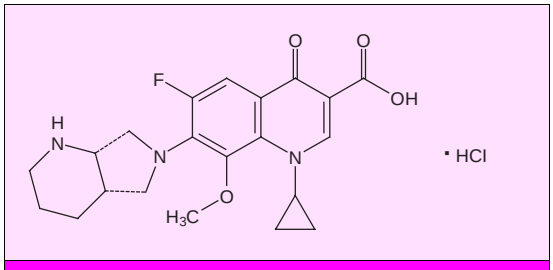
▲ In common with other fluoroquinolones, moxifloxacin attains good penetration into respiratory tissues and fluids and its bioavailability is substantially reduced by coadministration with an antacid or iron preparation. However, moxifloxacin does not interact with theophylline or warfarin.

▲ In clinical trials in patients with community-acquired pneumococcal pneumonia (CAP), acute exacerbations of chronic bronchitis (AECB) or acute sinusitis, moxifloxacin 400mg once daily achieved bacteriological and/or clinical success rates of approximately 90% or higher.

▲ Moxifloxacin was as effective as amoxicillin 1g 3 times daily and clarithromycin 500mg twice daily in CAP and as effective as clarithromycin in AECB. In patients with sinusitis, a 7-day course of moxifloxacin 400mg once daily was as effective as a 10-day course of cefuroxime axetil 250mg twice daily.

▲ In contrast to some other fluoroquinolones, moxifloxacin appears to have a low propensity for causing phototoxic and CNS excitatory effects. The most common adverse events are gastrointestinal disturbances.

Features and properties of moxifloxacin (BAY 12-8039)	
Indications	
Treatment of bacterial infections	Phase III
Mechanism of action	
Fluoroquinolone antibacterial agent	Bacterial DNA topoisomerase inhibitor
Pharmacokinetics (400mg oral dose)	
Peak plasma concentration	2.5 mg/L
Time to peak plasma concentration	1.5h
Renal/total clearance	3.03/14.9 L/h
Elimination half-life	≈9 to 16h
Dosage and administration	
Dosage	400mg
Route of administration	Oral
Frequency of administration	Once daily
Drug interactions	
Interact with moxifloxacin (decreased moxifloxacin absorption)	Antacids, iron preparations
No interaction with moxifloxacin	Theophylline, ranitidine, probenecid, warfarin
Adverse events	
Most frequent	Gastrointestinal disturbances



Moxifloxacin (BAY 12-8039)

Moxifloxacin, like other fluoroquinolone antibacterial agents, inhibits growth of susceptible bacteria by inhibiting bacterial DNA topoisomerases.

1. Antibacterial Activity

In Vitro Activity

The *in vitro* spectrum of moxifloxacin is broadly similar to that of other fluoroquinolones, although it has improved Gram-positive and anaerobe coverage compared with some of the older compounds, similar to trovafloxacin.[1]

In this review, *in vitro* antibacterial activity refers to minimum inhibitory concentrations (MICs) determined by broth or agar dilution techniques (except in the case of some intracellular bacteria, which were tested in cell culture). MIC_{50} and MIC_{90} refer to minimum concentrations required to inhibit 50 and 90% of strains, respectively. Proposed MIC susceptibility breakpoints for moxifloxacin indicating susceptibility and resistance are ≤2 and ≥4 mg/L, respectively.[2] Breakpoints for ciprofloxacin are as follows: susceptible MIC ≤1 mg/L; intermediately susceptible MIC 2 mg/L and resistant MIC ≥4 mg/L for organisms other than *Haemophilus* spp., *Neisseria gonorrhoeae* (susceptible MIC ≤1 and ≤0.06 mg/L, respectively) and *Streptococcus* spp. (not recommended).

Gram-Negative Bacteria

- Moxifloxacin showed good activity against Enterobacteriaceae, although it was generally approximately 2-fold less active than ciprofloxacin (fig. 1).[1,3] Although moxifloxacin was active against many strains of *Serratia marcescens* and β-lactam-resistant bacteria, including ampicillin- and ceftazidime-resistant *Escherichia coli* and ceftazidime-resistant *Klebsiella pneumoniae*, MIC_{90} values were >2 mg/L (fig. 1). This was also true for most other fluoroquinolones tested (ciprofloxacin, trovafloxacin, gatifloxacin, clinafloxacin, levofloxacin). Nevertheless, the majority of ceftazidime-resistant *K. oxytoca* strains were susceptible to moxifloxacin (MIC_{90} 0.25 mg/L) and other fluoroquinolones.[1]

- With regard to other Gram-negative organisms, some *Stenotrophomonas maltophilia* and *Pseudomonas* strains were susceptible to moxifloxacin but, in general, MIC_{90} values were ≥4 mg/L. Moxifloxacin was 4- to 8-fold less active than ciprofloxacin against *P. aeruginosa*, with MIC_{90} values of ≥32 mg/L[1,3] (fig. 2). Susceptible bacteria included *Aeromonas* spp., *Haemophilus influenzae* (including ampicillin-resistant strains), *Moraxella catarrhalis*, *Bordetella pertussis* and *Neisseria gonorrhoeae* (including ampicillin-resistant strains).[1,3]

- Moxifloxacin was more active than erythromycin against *Legionella* spp. (MIC_{90} 0.06 *vs* 0.12 mg/L; 27 strains).[4] It also showed good activity against *Mycoplasma* spp. (*M. pneumoniae*, *M. genitalium*, *M. hominis*, *M. fermentans* and *M. penetrans*; MIC_{90} 0.03 to 0.25 mg/L) and doxycycline-susceptible or -resistant *Ureaplasma urealyticum* (MIC_{90} 1 and 2 mg/L, respectively).[5]

- Moxifloxacin was slightly less active than ciprofloxacin against *Chlamydia pneumoniae* (49 strains; MIC range 0.125 to 4 *vs* 0.06 to 2 mg/L).[6] In a cell culture assay (10 strains), 90% of cells exposed to moxifloxacin 1 mg/L had no inclusions.[7]

Gram-Positive Bacteria

- Moxifloxacin was more active than ciprofloxacin against staphylococci (MIC_{90} 0.06 to 0.13 *vs* 0.5 to 1.0 mg/L, except for some methicillin-resistant strains) and streptococci (0.13 to 0.5 *vs* 1 to 4 mg/L; fig. 3). Its activity against these organisms was similar to that of trovafloxacin and 2- to 8-fold better than that of levofloxacin (data not shown).[1]

- In particular, moxifloxacin showed good activity against penicillin-susceptible and -resistant

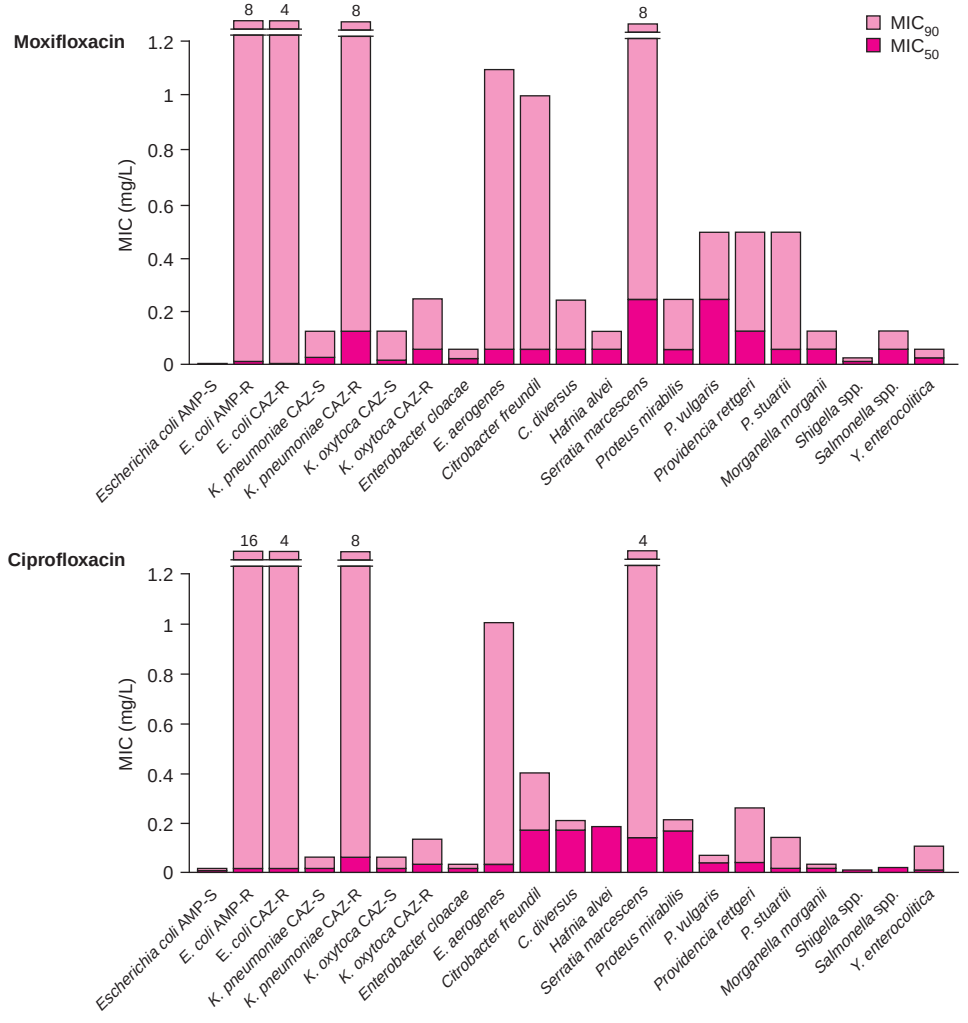


Fig. 1. *In vitro* activity of moxifloxacin and ciprofloxacin against Enterobacteriaceae (≈770 isolates).[1] **AMP-S** = ampicillin MIC ≤8 mg/L; **AMP-R** = ampicillin MIC ≥ 16 mg/L; **CAZ-S** = ceftazidime MIC ≤ 8 mg/L; **CAZ-R** = ceftazidime MIC ≥ 16 mg/L; **MIC_{50}** and **MIC_{90}** = minimum concentrations required to inhibit 50 and 90% of strains; where these values are off the scale they are shown above the relevant bar.

Streptococcus pneumoniae,[1,8-10] with MICs of ≤0.03 to 2 mg/L (MIC_{90} 0.125 mg/L) against 452 isolates (36 of which were highly resistant to penicillin). Moxifloxacin and trovafloxacin were generally 8-fold more active than ciprofloxacin and levofloxacin against these strains.[9]

- Against enterococci, moxifloxacin was again more active than ciprofloxacin (MIC_{90} 1 to 4 *vs* 4 to 16 mg/L; fig. 3).[1]
- Against *Mycobacterium tuberculosis* (n = 20, including 5 multidrug-resistant strains), moxifloxacin had similar activity to sparfloxacin (MIC_{90} 0.5 mg/L).[11]

Anaerobes

- When tested against 410 clinically important anaerobic bacteria, moxifloxacin inhibited 90% of strains at 2 mg/L.[12] *Clostridium*, *Fusobacterium*, *Eubacterium*, *Prevotella* and *Peptostreptococ-*

cus spp., *Propionibacterium acnes* and some *Bacteroides* spp. were all susceptible (MIC_{90} ≤2 mg/L).[1,3,12,13]

• Moxifloxacin was 16-fold more active than ciprofloxacin against *C. difficile* (MIC_{90} 2 *vs* 32 mg/L) and 4-fold more active against *Bacteroides fragilis*. (MIC_{90} 2 *vs* 8 mg/L; fig. 4). Moxifloxacin was also more active than ciprofloxacin against *Prevotella*, *Fusobacterium* and *Peptostreptococcus* spp. (MIC_{90} 0.25 to 2 *vs* 0.5 to 16 mg/L).[12]

Influence of Serum and Inoculum Size

• Increasing the inoculum size from 10^4 to 10^6 cfu did not influence MIC values for most strains tested; however, 2- to 4-fold increases in MIC were seen with some strains (*K. pneumoniae*, *Proteus mirabilis*, *S. marcescens*).[14] The antibacterial ac-

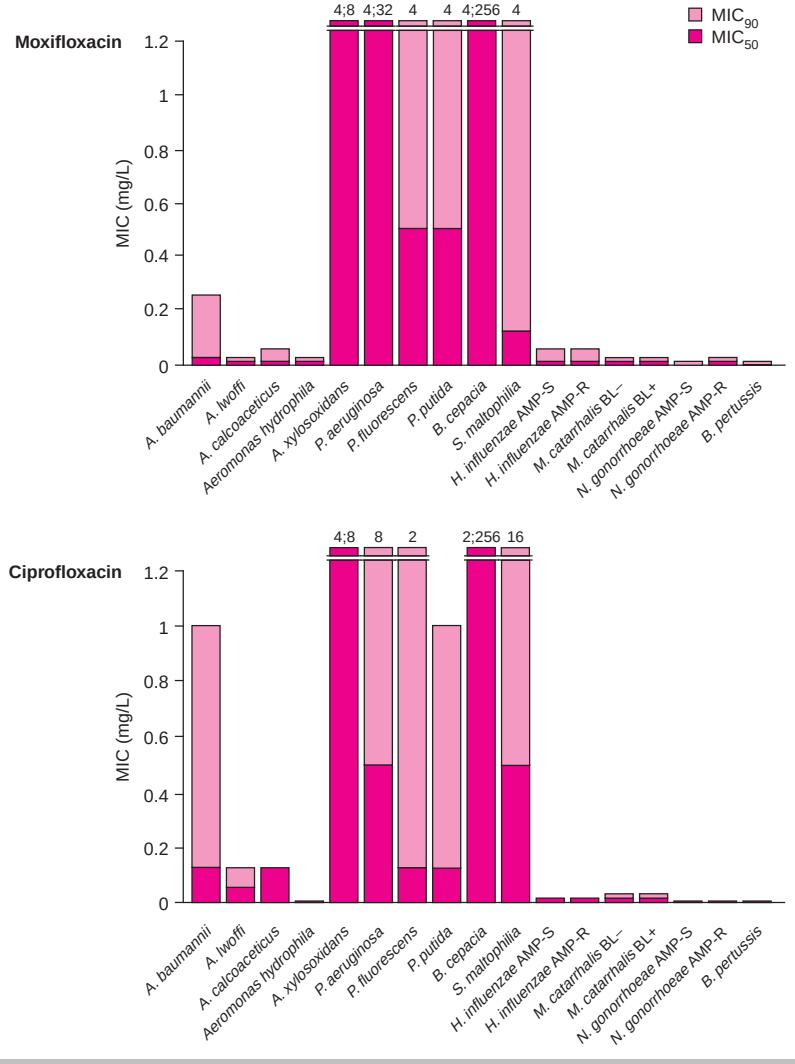


Fig. 2. *In vitro* activity of moxifloxacin and ciprofloxacin against other Gram-negative bacteria (≈490 isolates).[1] **AMP-S** = ampicillin MIC ≤8 mg/L; **AMP-R** = ampicillin MIC ≥ 16 mg/L; **BL–** = β-lactamase negative; **BL+** = β-lactamase positive; **MIC_{50}** and **MIC_{90}** = minimum concentrations required to inhibit 50 and 90% of strains; where these values are off the scale they are shown above the relevant bar.

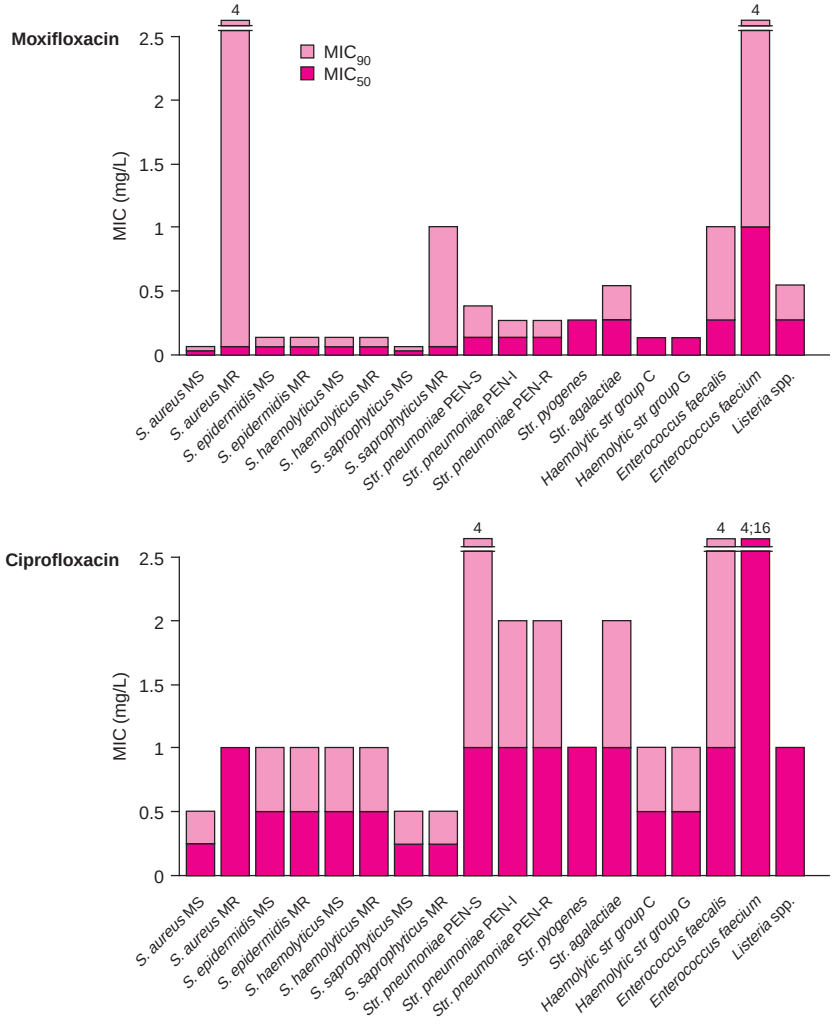


Fig. 3. *In vitro* activity of moxifloxacin and ciprofloxacin against Gram-positive bacteria (≈650 isolates).[1] **MIC_{50}** and **MIC_{90}** = minimum concentrations required to inhibit 50 and 90% of strains (where these values are off the scale they are shown above the relevant bar); **MS** = methicillin-susceptible; **MR** = methicillin-resistant; **PEN-I** = penicillin MIC 0.13-0.5 mg/L; **PEN-R** = penicillin MIC 1-4 mg/L; **PEN-S** = penicillin MIC ≤0.06 mg/L.

tivity of moxifloxacin was little affected by the presence of human serum (20 or 70%).[14]

Bactericidal Activity

- As with other fluoroquinolones, minimum bactericidal concentrations (MBCs) of moxifloxacin were equal to, or within 1 dilution of, MIC values.[14] In time-kill assays, moxifloxacin showed concentration-dependent killing at concentrations similar to the MIC against *S. pneumoniae*.[10] 99.9% killing in <2 hours was achieved at the MIC with *E. coli* and at 4 × MIC with *S. aureus*.[15]

Intracellular Activity

- At 10 × MIC, moxifloxacin was bactericidal against intracellular *S. aureus* engulfed within human phagocytes. 50% of a culture of a methicillin-

and ciprofloxacin-resistant strain was killed within 4 hours.[16]

Postantibiotic Effects

- At 4 × MIC, moxifloxacin showed postantibiotic effects (PAEs) of >1 hour (1.2 to 3.1 hours) against *E. coli*, *S. aureus*, *H. influenzae*, *S. pyogenes* and *S. pneumoniae*.[15] PAE was 2.3 hours against *S. pneumoniae* and 2.8 hours against *H. influenzae*. At 10 × MIC, PAEs were extended to 3.3 and 3.5 hours, respectively. No significant differences in PAE were noted between penicillin-susceptible and -resistant strains.[17]

In Vivo Activity

- In experimental lung infections in guinea-pigs,[18] or mice[19,20] moxifloxacin (10 to 100 mg/kg) eradicated or markedly reduced the number of *M. pneumoniae*,[18] *S. pneumoniae*[19,20] or *C. pneumoniae*[20] in the lung. Pneumococci were completely eradicated from the lung in 11 of 15 animals.[19]

- Moxifloxacin (100 mg/kg/day; route of administration not stated) also reduced bacterial counts in the organs in a murine model of *M. tuberculosis* infection. After 4 weeks, bacterial counts were significantly reduced ($p < 0.001$) versus the control group in the lungs ($10^{0.6}$ *vs* $10^{5.6}$ cfu) and spleen ($10^{1.5}$ *vs* $10^{4.9}$ cfu). Lungs were sterile at 8 weeks in 7 of 8 mice.[21] In a similar model, moxifloxacin (100 mg/kg 6 times weekly), but not sparfloxacin or clinafloxacin, was bactericidal, with activity similar to isoniazid (25 mg/kg 6 times weekly).[11]

- In experimental models of *S. pneumoniae* meningitis in rabbits, intravenous moxifloxacin rapidly reduced bacterial counts in the CSF.[22,23] Moxifloxacin 10 mg/kg/h was as active as ceftriaxone (10 mg/kg/h) against infection caused by a penicillin-susceptible pneumococcal strain,[22] and 2 doses of moxifloxacin 20 or 40 mg/kg were as active as vancomycin (two 20 mg/kg doses) or ceftriaxone (125 mg/kg) against a penicillin-resistant strain.[23] Both doses of moxifloxacin sterilised the CSF in 5 of 5 animals by 24 hours.[23] The dosage of moxifloxacin required to reduce bacterial counts by 50% was estimated to be 1.4 mg/kg/h.[22]

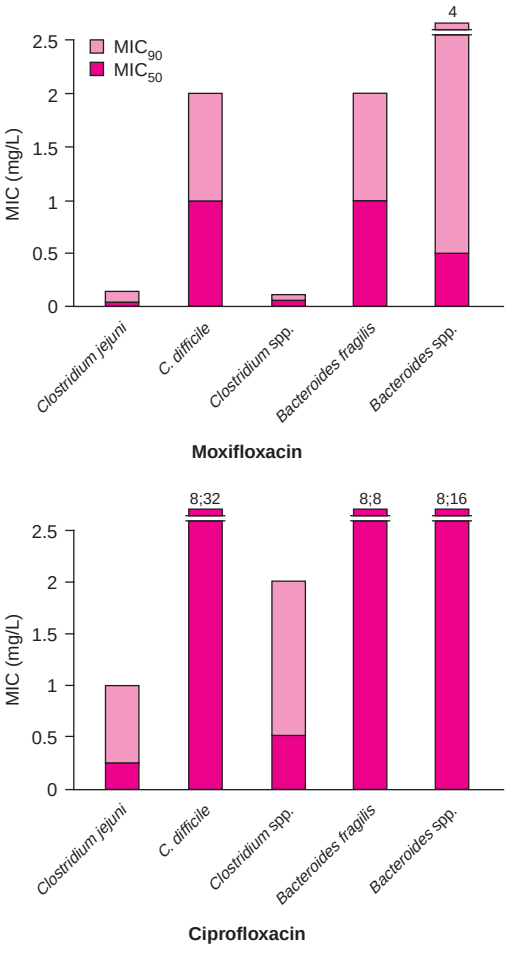


Fig. 4. *In vitro* activity of moxifloxacin and ciprofloxacin against anaerobes (≈70 isolates).[1] **MIC_{50}** and **MIC_{90}** = minimum concentrations required to inhibit 50 and 90% of strains; where these values are off the scale they are shown above the relevant bar.

Resistance Issues

- In Gram-positive bacteria, resistance to moxifloxacin developed less frequently and more slowly than resistance to 3 other fluoroquinolones. At 4 × MIC, the frequency of spontaneous mutation in *S. pneumoniae* was 1.45×10^{-9}, compared with $<10^{-8}$ for ofloxacin and grepafloxacin and 9.8×10^{-8} for trovafloxacin.[24] At 8 × MIC, the frequency of spontaneous resistance to moxifloxacin among typical respiratory tract pathogens was <4

$\times 10^{-8}$.[25] Cross-resistance between moxifloxacin and other fluoroquinolones was demonstrated in Gram-negative bacilli and enterococci.[26] Nevertheless, of 5 fluoroquinolones tested, moxifloxacin was the least affected by mutations at the *grlA*, *grlB*, *gyrA* and *gyrB* loci in *S. aureus* isolates, inhibiting ciprofloxacin-resistant *S. aureus* at a concentration of 0.5 to 2 mg/L. Rank order of MICs was ciprofloxacin>ofloxacin>levofloxacin > sparfloxacin>moxifloxacin.[27]

- In the rat granuloma pouch model, resistance to moxifloxacin did not develop in infecting *S. aureus* or *S. pneumoniae* strains during administration of suboptimal doses or oral doses that simulated human serum kinetics.[28]

2. Pharmacokinetic Profile

Absorption and Distribution

- Peak plasma concentrations (C_{max}) and area under the plasma concentration-time curve (AUC) increased linearly with dose after administration of single oral moxifloxacin doses of 50 to 800mg to healthy volunteers (n = 45). After the recommended dose of 400mg, a mean C_{max} of 2.5 mg/L was reached in 1.5 hours (t_{max}) and AUC was 26.9 mg/L · h.[29]

- Repeated administration of moxifloxacin 400 mg/day orally for 10 days to healthy volunteers (n = 10) resulted in a C_{max} of 4.52 mg/L and an accumulation ratio of 1.59 on day 10.[30]

- Intravenous administration of moxifloxacin 400mg produced a C_{max} of 3.62 mg/L and AUC of 34.6 mg/L · h.[31]

- The absolute bioavailability of oral moxifloxacin was 89%.[32] Concomitant intake of dairy products slightly delayed the rate, but not the extent, of absorption of the drug.[33]

- The volume of distribution of moxifloxacin was 3.55 L/kg.[29] The drug was 48% bound to plasma proteins.[29]

- Moxifloxacin penetrated efficiently into interstitial compartments in healthy volunteers (n = 13). Concentrations in skin blister fluid were approximately 2-fold higher than concurrent serum concentrations 24 hours after a single 400mg oral or intravenous dose.[32]

- Concentrations of moxifloxacin in epithelial lining fluid and bronchial biopsies (24.4 and 5.5 mg/L at 1 hour after administration) exceeded those in plasma, in 18 patients who received a single oral 400mg dose before bronchoscopy. The drug was highly concentrated within macrophages, reaching concentrations of 113.6 mg/L at 12 hours.[34]

- Moxifloxacin also showed good penetration into sinus tissues. In 34 patients with chronic sinusitis who received 5 oral 400mg doses of moxifloxacin before undergoing surgery, drug concentrations in maxillary sinus mucosa exceeded those in plasma, ranging from a maximum of 7.47 mg/kg at 3 hours, to 1.25 mg/kg at 36 hours, postdose. Similar results were noted in anterior ethmoid mucosa and nasal polyp tissue.[35]

- In animal studies, orally administered moxifloxacin penetrated across the placental barrier and into breast milk in rats,[36] and achieved good penetration into CSF in rabbits, particularly in those with experimental meningitis.[22,23] C_{max} in the CSF was approximately 4 mg/L after 4 doses of 10 mg/kg.[23]

Metabolism and Elimination

- Total and renal clearance of moxifloxacin were 14.9 and 3.03 L/h, respectively, after administration of a single oral 400mg dose to healthy volunteers.[29] In rats, 68% of a radiolabelled intravenous dose of moxifloxacin was excreted in the bile.[37]

- Moxifloxacin does not appear to be metabolised by the P-450 pathway.[38] Metabolites formed by human hepatocytes *in vitro* are the *N*-sulfate and acyl glucuronide.[39] The good correlation observed between microbiological and high performance liquid chromatography assay results suggests that the metabolites do not have any major antimicrobial activity.[29]

- The mean elimination half-life ($t_{½\beta}$) of moxifloxacin in healthy volunteers was 9.3 hours on day 1 and 11.95 hours on day 10 of repeated administration (400 mg/day orally).[30] In other studies,

mean $t_{½\beta}$ ranged from approximately 10 to 16 hours.[29,31,40]

- Urinary recovery of moxifloxacin was approximately 19 to 20% after a single oral dose,[29,31] and 22% after a single intravenous dose,[31] of 400mg.

Influence of Age and Disease on Pharmacokinetics

- Disposition of moxifloxacin did not appear to be significantly affected by advanced age or gender. In a study involving 3 groups of 12 volunteers, C_{max} and AUC values were higher in elderly women than in elderly men (mean age of both 74 years) and young men (1.9 and 25.2 *vs* 1.6 and 19.9 *vs* 1.4 mg/L and 19.1 mg/L · h). However, no significant differences between groups were noted after normalisation of these parameters for bodyweight.[41]

- Renal impairment did not affect the oral clearance of moxifloxacin in 32 volunteers with CL_{CR} <1.8 to >5.4 L/h/1.73m^2 who received a single oral 400mg dose. However, renal clearance of the drug decreased as a function of creatinine clearance (CL_{CR}). Thus, dosage reduction does not appear to be necessary in patients with renal dysfunction,[42] although multiple dose studies are required to confirm this.

3. Therapeutic Trials

Moxifloxacin 400mg once daily has been evaluated in the treatment of respiratory tract infections, including community-acquired pneumonia (CAP), acute exacerbations of chronic bronchitis (AECB) and acute sinusitis. All studies except one were reported as abstracts and few details of methodology and results are available. In particular, clinical and bacteriological success were not defined. The dosage of clarithromycin used was generally not stated, but was 500mg twice daily.[43]

Community-Acquired Pneumonia

- Moxifloxacin was as effective as amoxicillin 1g 3 times daily in 411 patients (362 evaluable) with a presumptive diagnosis of pneumococcal CAP in a randomised, double-blind multicentre study.[44] Both treatments were given for 10 days. Clinical success was achieved in 91.5% of moxifloxacin and 89.7% of amoxicillin recipients, with bacteriological cure in 89.7 and 82.4% of patients. 94.4% of moxifloxacin- and 86.7% of amoxicillin-treated patients infected with *S. pneumoniae* strains which were intermediately susceptible or resistant to penicillin were clinically cured. Clinical cure rates were maintained at 21 to 28 days after treatment (89% of patients in both groups).

- Meta-analysis of data from 243 patients with CAP participating in 5 multinational studies and treated with moxifloxacin, amoxicillin (dosage not stated) or clarithromycin (500mg twice daily) showed that bacteriological success was achieved in 96, 86 and 90% of patients, respectively. In moxifloxacin-treated patients, 100% of *S. aureus* (n = 8) and *H. influenzae* (n = 24), 94% of *S. pneumoniae* (n = 42) and *M. catarrhalis* (n = 6) and 89% of *K. pneumoniae* (n = 7) strains were eradicated. Moxifloxacin was particularly effective against infections caused by penicillin- and macrolide-resistant pneumococci, with success rates (not defined) of 92 and 100% against highly penicillin-resistant (MIC ≥2 mg/L) and clarithromycin-resistant (MIC ≥2 mg/L) strains.[45]

Acute Exacerbations of Chronic Bronchitis

- 750 patients with AECB participated in a randomised, double-blind study comparing a 5-day course of moxifloxacin with a 7-day course of clarithromycin 500mg twice daily. Clinical cure was documented in 89% (287 of 322) of moxifloxacin and 88% (289 of 327) of clarithromycin recipients at the end of treatment, and in 89% of patients in both treatment groups at 21 to 28 days after treatment. Of the 342 pathogens isolated from sputum, the most common were *H. influenzae* (37%) *S. pneumoniae* (31%) and *M. catarrhalis* (18%). Moxifloxacin was reported to be more effective bacteriologically than clarithromycin, particularly against *H. influenzae*, but details were not presented.[46]

• Meta-analysis of data from 4 multinational studies in patients with AECB showed that moxifloxacin was more effective than clarithromycin (500mg twice daily) in eradicating *H. influenzae* (97 *vs* 72% of strains; p value not stated). 96 to 98% of *S. pneumoniae*, *H. parainfluenzae* and *M. catarrhalis* were eradicated after moxifloxacin treatment and clinical success was documented in 92 to 100% of patients (data for clarithromycin not reported).[47]

Acute Sinusitis

• A 7-day course of moxifloxacin was compared with a 10-day course of cefuroxime axetil 250mg twice daily in a randomised, double-blind multicentre study in patients with acute bacterial sinusitis. Complete resolution of clinical symptoms was achieved in 216 of 242 (89%) moxifloxacin and 219 of 251 (87%) cefuroxime axetil, recipients in the intent-to-treat population and in 204 of 211 (97%) versus 204 of 225 (91%) of the evaluable population. At 3- to 4-week follow-up, 91 versus 89% of patients were judged as successfully treated. Bacteriological success without superinfection was achieved in 103 of 109 patients (95%) in the moxifloxacin group versus 96 of 115 patients (84%) of the cefuroxime axetil group.[48]

• Meta-analysis of data from 4 multinational studies in patients with acute sinusitis treated with moxifloxacin showed that bacteriological and clinical success were each achieved in 96% of 282 evaluable patients. 89 to 97% of *S. pneumoniae* (n = 35), *S. aureus* (n = 7), *H. influenzae* (n = 23) and *M. catarrhalis* (n = 23) were eradicated.[49]

4. Tolerability

• Meta-analysis of data from 20 phase II and III studies involving 4926 patients treated with moxifloxacin (mostly 400 mg/day) indicated that adverse events were mostly mild and transient and led to discontinuation of treatment in 3.8% of patients. The most frequent events were nausea (7.2%) and diarrhoea (5.7%). Dizziness occurred in 2.8% of patients and drug-related phototoxicity did not occur.[50] However, this report was presented as an abstract and few details are available.

• Moxifloxacin (single doses of 50 to 800mg or multiple doses up to 600mg once daily for 10 days) did not cause any clinically relevant changes in vital signs, haematology, blood chemistry or ECG in healthy volunteers (n = 103). The most common adverse events were nausea and loose stools.[51]

Phototoxic and Central Nervous System Excitatory Potential

• Electrophysiological testing in rat hippocampal slices indicated that moxifloxacin had a relatively low potential, similar to that of ciprofloxacin, for producing CNS adverse effects. At a concentration of 2 μmol/L, moxifloxacin increased the population spike amplitude to 170% of control, compared with 155% for ciprofloxacin, 192% for enoxacin and 233% for clinafloxacin.[52]

• In contrast with lomefloxacin, moxifloxacin (200 or 400 mg/day) did not produce any measurable phototoxicity in a double-blind, placebo-controlled phototest study in 32 volunteers.[53] Similarly, no ultraviolet-dependent increase of skin reddening was seen in guinea-pigs and rats given moxifloxacin (30 to 100 mg/kg), whereas sparfloxacin produced a pronounced and long-lasting skin reaction after irradiation. Studies with 3T3 mouse fibroblasts supported these findings; moxifloxacin did not induce any cytotoxicity with or without ultraviolet irradiation.[54]

5. Drug Interactions

• As with other quinolones, the bioavailability of moxifloxacin (400mg) was substantially reduced when it was coadministered with an antacid (Maalox® 3 times daily). AUC and C_{max} were decreased to 45 and 40% of values measured with moxifloxacin alone. Administration of the antacid 2 hours before, or 4 hours after, moxifloxacin did not significantly affect absorption of the quinolone.[55]

• Concomitant administration of an iron preparation (Erifer®) with moxifloxacin 400mg signifi-

cantly decreased absorption of the fluoroquinolone; AUC and C_{max} were reduced by 39 and 59%, respectively.[56]

- However, moxifloxacin did not show any clinically relevant interaction with theophylline,[57] probenecid,[58] ranitidine[59] or warfarin.[60]

6. Moxifloxacin: Current Status

Moxifloxacin is currently in phase III clinical studies in Europe and the US for treatment of bacterial infections, including respiratory tract and skin and soft tissue infections.

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